REMARKS

The foregoing amendments and the following remarks are submitted in response to the communication dated October 19, 2004.

Status of the Claims

Claims 14-17 are pending in the application. Claims 14 and 15 have been amended in order to more particularly point out and distinctly claim that which Applicants regard as the invention. Support for the amended claims can be found generally through Applicants' specification.

Particularity and Distinctiveness of the Claims

The Examiner has rejected claim 14 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter applicant regards as the invention. The Examiner asserts that claim 14 is unclear because it fails to recite that the cell is isolated. Applicants have above amended claim 14 to reference an "isolated" pluripotent embryonic-like stem cell.

In view of the foregoing amendment and remarks, Applicants submit that the Examiner's 112, second paragraph, rejection is obviated and should be withdrawn.

The §102 Rejections

The Examiner has rejected claims 14-16 under 35 U.S.C. 102(b) as being anticipated by Capecchi et al [Scientific American 270(3):34-41 (1994)]. Capecchi teaches the inactivation of target genes by homologous recombination and the insertion of a *neo* resistance gene, which serves as a positive selection marker, in mouse ES cells. The Examiner remarks that the claimed cells are not distinguished from those taught by Capecchi. Capecchi, it is asserted, fulfills the limitations of the claims (differentiation to cells of any endodermal, ectodermal, mesodermal lineage). Further, the Examiner asserts that if "the product in a product-by-process claim is the

same as or obvious from a product of the prior art, the claim is unpatentable, even though the prior product was made by a different process." Applicants respectfully disagree. Capecchi teaches ES cells, embryonic stem cells, which are totipotent cells, as noted and described in Applicants specification, including at page 3, lines 29-31:

> Embryonic stem cells are uncommitted, totipotent cells isolated from embryonic tissue. When injected into embryos, they can give rise to all somatic lineages as well as functional gametes. In the undifferentiated state these cells are alkaline phosphatase-positive, express immunological markers for embryonic stem and embryonic germ cells, are telomerase positive, and show capabilities for extended self-renewal.

Totipotent cells, as noted and defined, are capable of differentiation to cells of any endodermal, ectodermal, mesodermal lineage and also give rise to finctional gametes. The pluripotent embryonic-like stem cells of the present invention are pluripotent and are capable of differentiation to cells of any endodermal, ectodermal, mesodermal lineage, but are not totipotent – they do not give rise to functional gametes. This distinction is now recited in the claims as amended for clarification. Thus, the pluripotent embryonic-like stem cells of Applicants, as claimed, are not anticipated by the ES cells of Capecchi – they differ as a product, as well as being isolatable from a non-embryonic or postnatal cell (ie., made by a different process). The Capecchi et al reference does not teach or anticipate the stem cells identified and claimed by Applicants.

Claims 14-17 are rejected under 35 U.S.C. 102(b) as anticipated by Povey et al [Blood 92(11): 4080-4089 (1998)], which teaches the transfection of hematopoietic stem cells using a retroviral vector. The Examiner asserts that the instant claims fail to be distinguished from the cells taught by Povey which are hematopoietic stem cells capable of multilineage differentiation and self-renewal. Applicants disagree and argue that the transfected hematopoietic stem cells of Povey, capable of differentiation only to hematopoietic cells, which are one type of mesodermal cell, do not anticipate the claimed cells of the instant Application. The pluripotent embryonic-like stem cells of the instant Application are capable of differentiation to cells of each and any of endodermal, ectodermal and mesodermal germ layer lineages. Applicants' cells are not limited to one or two of the lineages but can differentiate to any cells of each and all three germ layer

lineages. Hematopoietic stem cells are a more differentiated and limited cell and do not teach or anticipate the stem cells of Applicants.

The Examiner rejects claims 14-17 under 35 U.S.C. 102(b) over Verma et al [Gene Therapy 5:692-699 (1998)], which describes the transfection of hematopoietic progenitor cells using a CMV-CAT reporter plasmid. The hematopoietic progenitor cells of Verma are able to differentiate into cells of only the hematopoietic lineage and do not anticipate the isolated pluripotent embryonic-like stem cells of the instant Application. The isolated pluripotent embryonic-like stem cells as claimed by Applicants are capable of differentiation to cells of each and any of endodermal, ectodermal and mesodermal germ layer lineages. Again, hematopoietic stem cells are a more differentiated and limited cell and do not in fact teach or anticipate the pluripotent embryonic-like stem cells of Applicants.

In view of the foregoing amendments and remarks, Applicants submit that the Examiner's 102 rejections are obviated and should be withdrawn.

The §103 Rejections

The Examiner maintains her prior rejection of claims 14-17 under 35 U.S.C. 103(a) over Pittenger et al [Science 284:143-147 (1999)] in view of Sambrook et al [Molecular Cloning, Book 3, 1989]. Pittenger teaches human mesenchmyal stem cells which are found to differentiate into multiple mesenchmyal lineages *in vitro*. Sambrook teaches methods of transfecting mammalian cells with any gene of interest. The Examiner asserts that the claims are written in the alternative, and do not require differentiation into all three lineages, endodermal, ectodermal and mesodermal. Applicants respectfully disagree and submit that the cells as claimed by Applicants are not obvious over Pittenger in view of Sambrook. The human mesenchmyal stem cells of Pittenger are capable of differentiating into cells of only the mesenchmyal lineage. Applicants have above amended claims 14 and 15 to clarify the language and intent of the claims to properly reference and include the novel capabilities of the pluripotent embryonic-like stem cells of the instant invention. The pluripotent embryonic-like stem cells of

this Application, as claimed, are capable of differentiation to cells of each and any of the lineages ectodermal, endodermal and mesodermal. This differentiation capacity is not in the alternative and is not anticipated or made obvious by stem cells capable of differentiating into only a single or even two lineage type(s). As described in the Specification, including at page 53, lines 25-27:

> Thus, cells of any of the endodermal, ectodermal and mesodermal lineages can be provided from a single, self-regenerating source of cells obtainable from an animal source even into and through adulthood.

The cells of Pittenger, mesenchmyal stem cells, have a limited differentiative capacity to only mesenchymal lineage cells and do not, when combined with the teachings of Sambrook, render the pluripotent embryonic-like stem cells claimed by Applicants obvious.

Claims 14-17 are further rejected under 35 U.S.C. 103(a) over Shamblott [PNAS 95:13726-13731 (1998)] in view of Sambrook et al [Molecular Cloning, Book 3, 1989]. Shamblott et al teach the generation of human pluripotent stem cells from gonadal ridges and mesenteries containing primordial germ cells (PGCs) and teach that embryoid bodies collected from these cultures revealed a wide variety of differentiated cell types, including derivatives of all three embryonic germ layers. Sambrook teach methods of transfecting mammalian cells with any gene of interest. The Examiner remarks that the instant claims do not provide any requisite characteristics (e.g. specific markers) of the claimed stem cells such that they would be distinguished from the cells taught by Shamblott. Applicants respectfully disagree and assert that the cells identified and claimed by Applicants are not rendered obvious by the combination of the Shamblott and Sambrook references. The pluripotent embryonic stem cells are distinct from embryonic stem cells and primordial germ cells, particularly in that they are pluripotent and are are not totipotent – they do not give rise to functional gametes.

The Examiner rejects claims 14-17 under 25 U.S.C. 103(a) as being unpatentable over Thomson [Reference BR on Applicants' IDS filed 7/3/03, PNAS USA 92:7844-7848 (1995)] taken with Sambrook [Molecular Cloning, Book 3, 1989]. Thomson teaches the isolation of embryonic stem (ES) cells from the rhesus monkey, which differentiated into cells of endoderm,

mesoderm and ectoderm. Sambrook teaches methods of transfecting mammalian cells with any gene of interest. Applicants again assert that the claimed pluripotent embryonic-like stem cells are distinct and unobvious from ES cells, and are also not made obvious by the combination of ES cells taught in Thomson with the transfection of mammalian cells taught by Sambrook. ES cells are totipotent and are capable of giving rise to all somatic lineages (ectodermal, endodermal and mesodermal) as well as functional gametes. The pluripotent embryonic-like stem cells of the present invention are pluripotent and are capable of differentiation to cells of any endodermal, ectodermal, mesodermal lineage, but are not totipotent – they do not give rise to functional gametes. The combination of Thomson and Sambrook does not make obvious the genetically engineered pluripotent embryonic-like stem cells as claimed by Applicants.

In view of the foregoing amendments and remarks, Applicants submit that the Examiner's 103 rejections are obviated and should be withdrawn.

CONCLUSION

Applicants respectfully request entry of the foregoing amendments and remarks in the file history of the instant Application. The Claims as amended are believed to be in condition for allowance, and reconsideration and withdrawal of all of the outstanding rejections is therefore believed in order. Early and favorable action on the claims is earnestly solicited.

Respectfully submitted,
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